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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/852,910	05/11/2001	Annette Gilchrist	2661-101	4758

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/852,910	GILCHRIST ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-9 and 12-102* is/are pending in the application.

4a) Of the above claim(s) *2, 12, 20, 25-32 and 34-102* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-9,13-19,21-24,33 and 102* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of the species, Seq. ID. 38 in the reply filed on 3/8/2006 is acknowledged.

Status of Claims

Claims 1-3, 5-9 and 12-102 are pending in the application.

Claims 2, 12, 20, 25-32 and 34-102 (with respect to the non-elected species. Note claim 42 is a DNA sequence) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and specie, as stated above.

Claims 1, 3, 5-9, 13-19, 21-24, 33 and 102(with respect to the elected Seq. ID. 38) are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1, 3, 5-9, 13-19, 21-24, 33 and 102, as amended, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method utilizing a biased library based from a native G protein Gα-subunit carboxyl terminal and specific peptide library for the candidate compounds does not reasonably provide enablement for a method

using any or all types of a native Gα-subunit carboxyl terminal for the peptide library or candidate compounds for reasons advanced in the last Office action.

Response to Arguments

Applicants argue that the Office is rejecting methods to a screening method based on an inability to disclose in advance all compounds which could be screened using the method.

In response, in order to screen millions of compounds present in a library, the structure of the library, at least, has to be given to enable its screening and obtain the desired compound. However, given no structure of the peptide except that it is based on the native G protein G alpha subunit carboxyl terminal peptide it is not apparent how one can proceed with the screening process. It does not recite the length of the variant peptide, the numerous native G-protein from which it is based and the other distinguishing features that would lead one skilled to the genus library of such huge scope.

Applicants argue that it is not proper to limit the claims to a single example based on applicants' statement that Seq. ID. No. 139 is an example of what the exemplary libraries were based on.

In reply, applicants have not been required to limit the claims to a single example. Rather applicants are required by

law to provide guidance and reasonable assurance that the exemplary Seq. ID. No. 139, would be considered representative of the huge genus of the library as claimed.

Applicants argue that the library works as evident from Example 24 for at least, G alpha q, 11, s, t, 12 and 13 that results in the peptide product in tables IV-V and IX-XVIII. Applicants further argue the different G alpha based library binds to the specific GPCR e.g., B2 adrenergic receptor.

In reply, the species of the recited G alpha is not controverted. The issue is the huge scope of a library of variant peptides based on the primary sequence of a native G alpha subunit carboxyl terminal peptide. The specification does not recite the numerous G protein containing G alpha subunit carboxyl peptide sequences. It also does not describe the numerous variations of the different peptide sequences in each of the different G alpha subunit of a native G protein that results in a variant peptide library.

Applicants acknowledge that although G alpha peptide could be used in the screen, the claims still are limited to G alpha peptide that binds to GPCR.

In reply, GPCR is in itself a huge scope of receptors, let alone any G alpha that binds to it. It is well known in the art that some peptides in the library might not be the desired

binding peptide. Some peptides in the library may not be expressed at all or underrepresented in the library to be functional in its binding effect.

Applicants state that a single native G protein has only one G alpha. Sometimes this G alpha is G alpha t. Applicants further state that what species and what genus this hypothetical listing would not be enabled is not explained by the examiner.

In reply, as acknowledged by applicants, a single native protein G alpha covers numerous subsets e.g., G alpha t, i, o, s, q, 11, 12, 13. 14 and so on. This is not to mention the variations for each of these subsets to form a library. A hypothetical list of the compound is not a full, clear, concise and exact description, as required by the law. It would not lead one skilled in the art to the actual library.

Applicants submit that the scope is broad only in the sense that the screen can work with any GPCR/G alpha pair that binds, but not broad in that any GPCR should be screened with any G alpha peptide whether it binds that GPCR or not.

In reply, as acknowledged by applicants, the scope is broad in the sense of screening GPCR/G alpha pair that binds. The two representative examples of the receptors e.g., PAR1 and b-adrenergic receptors for the G alpha subunit would not be considered representative for any GPCR. Furthermore, G alpha

binding peptide is but one of the numerous undefined compounds of the claim. There is yet a claim to an inhibitor in a library of candidate compounds. It is not apparent as to the small molecule identified that competes with the selected G alpha subunit in binding to GPCR.

Applicants cannot understand why G alpha t is a huge species from one type of G alpha.

In response, G alpha t, in and of itself, would cover numerous variations e.g., additions, deletions, substitutions, singly or in multiples of each of the amino acids based on the parent G alpha subunit. This is not to mention, the other numerous undefined structures of the method component e.g., library of candidate compounds.

Applicants refer to Examples 37-38 for molecules screened for activity and specificity.

In response, the Examples in the specification end with Example 33. There is no Examples 37-38.

Applicants' lengthy arguments with respect to the interaction of GPCR and the G alpha subunits are noted. However, the issue here is not only the interactions between these two proteins. The claïm calls for a two-screen method i.e., a yet undefined library of candidate compounds. Example 33 of the specification proposes the use of small library of molecules

purchased from a vendor, Chem. Div. It is not apparent just what exactly the composition of said purchased small library of molecules. More importantly, the small molecules found to compete with the library of G alpha subunit for the method to work.

Applicants argue that claim 120 has been added to add the limitation of the different G alpha based sequences to form the library.

In reply, it is not clear how the recited sequences form a G alpha based library. Cf. with the library at page 23, Table I and page 50, Table VI.

Claims 1, 3, 5-9, 13-19, 21-24, 33 and 102 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. [This is a new matter issue].

The claimed "in the presence of said native G protein G alpha subunit carboxyl terminal peptide" is not supported in the as-filed specification. MPEP 714.02 states that applicants point

out specifically where in the specification the new limitation can be found. (See further the rejection immediately below).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 5-9, 13-19, 21-24, 33 and 102, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 1 step (b) is indefinite. Does the peptide library compete with the added ***native*** G protein G alpha carboxyl terminal peptide to have the claimed "higher" affinity?

2. Claim 120 is confusing as to whether the recited amino acid sequences, for example, Seq. ID. No. 13 is varied or the expressed or obtained peptide. See page 71, Table XVIII. Cf. with page 23, Table I and page 50, Table VI.

Claim Rejections - 35 USC § 103

Claims 1, 3, 5-9, 13-19, 21-24, 33 and 102, as amended, are rejected under 35 U.S.C. 103(a) as being obvious over Fowlkes et

al (WO 98/19162) in view of Gilchrist (The Journal of Biological Chemistry) for reasons set forth in the Office action.

Response to Arguments

`Applicants acknowledge the two steps of screening as proposed by Fowlkes. But argue that discovering high affinity binders is not even a goal in Fowlkes et al. It is further argued that Fowlkes acknowledge that the interactions they hope to study with their methods will likely be of considerably lower affinity than the native interactions (see page 79, lines 9-12). The methods claimed here identify higher affinity compounds to reduce false positives by identifying only high affinity peptides and compounds.

In response, it is well known in the art that the only goal of screening a compound is to obtain a better (lead compound) e.g., higher affinity binders in comparison with the native one. See the Gilchrist reference e.g., Table 1, page 14914 and the RESULTS section. Applicants have taken the disclosure of Fowlkes at page 79 of out of context. Fowlkes states "…it is possible that most if not all peptide processivity factor interactions ***will be of considerably lower affinity*** that the polymerase-processivity factor or DNA …interaction, ***but we can use a vast excess of the peptide to drive the peptide interaction to search for effects……"*** (Emphasis added). It would be within the ordinary

skill in the art to screen for higher affinity compounds, since this is the main goal of any screening process. Screening, as practiced in the art results in a compound with a better affinity or binding compounds that gives a lead (drug) compound.

Applicants argue that Fowlkes describes screening protein generally for binding to any site on the protein, trusting that a site having potential interest will be bound by some of the screened peptides. The individual peptides would have to be tested for activity. The inventive methods do not require this type of confirmation because the screen is specific for a site already known to be of interest that has an already known native binding sequence.

In response, applicants' method is no different from the screening method of Fowlkes i.e., the hope that some binders higher than the native would bind from the collection of numerous compounds (library). It also requires identifying one that has a higher affinity than the native one, even if the site is already known. It is well known in the art that with the millions of compounds in a library, underrepresentation of some compound can occur, even with a specific one. All screening in essence is a "fishing expedition".

Claim 120 e.g., Seq. ID. 13, 15, 17 and 21 is obvious over the disclosure of Gilchrist at Table 1.

The elected species is free of prior art hence, the search was extended to the other species.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 2, 12, 20, 25-32 and 34-102 drawn to a nonelected invention. A complete reply to the

final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
May 24, 2006